Osteoporosis drug stops growth of breast cancer cells, even in resistant tumors

June 15 2013

A drug approved in Europe to treat osteoporosis has now been shown to stop the growth of breast cancer cells, even in cancers that have become resistant to current targeted therapies, according to a Duke Cancer Institute study.

The findings, presented June 15, 2013, at the annual Endocrine Society meeting in San Francisco, indicate that the drug bazedoxifene packs a powerful one-two punch that not only prevents estrogen from fueling breast cancer cell growth, but also flags the estrogen receptor for destruction.

"We found bazedoxifene binds to the estrogen receptor and interferes with its activity, but the surprising thing we then found was that it also degrades the receptor; it gets rid of it," said senior author Donald McDonnell, PhD, chair of Duke's Department of Pharmacology and Cancer Biology.

In animal and cell culture studies, the drug inhibited growth both in estrogen-dependent breast cancer cells and in cells that had developed resistance to the anti-estrogen tamoxifen and/or to the aromatase inhibitors, two of the most widely used types of drugs to prevent and treat estrogen-dependent breast cancer. Currently, if breast cancer cells develop resistance to these therapies, patients are usually treated with toxic chemotherapy agents that have significant side effects.

Bazedoxifene is a pill that, like tamoxifen, belongs to a class of drugs

known as specific estrogen receptor modulators (SERMs). These drugs are distinguished by their ability to behave like estrogen in some tissues, while significantly blocking estrogen action in other tissues. But unlike tamoxifen, bazedoxifene has some of the properties of a newer group of drugs, known as selective estrogen receptor degraders, or SERDs, which can target the estrogen receptor for destruction.

"Because the drug is removing the estrogen receptor as a target by degradation, it is less likely the cancer cell can develop a resistance mechanism because you are removing the target," said lead author Suzanne Wardell, PhD, a research scientist working in McDonnell's lab.

Many investigators had assumed that once breast cancer cells developed resistance to tamoxifen, they would be resistant to all drugs that target the estrogen receptor, McDonnell explained.

"We discovered that the estrogen receptor is still a good target, even after it resistance to tamoxifen has developed," he said.

The investigators tested a variety of breast cancer cell types, including tamoxifen-sensitive cells that are resistant to the drug lapatinib, another targeted therapy that is used to treat patients with advanced breast cancer whose tumors contain the mutant HER2 gene. These cells had previously been shown to reactivate estrogen signaling in order to acquire drug resistance. In this cell type, bazedoxifene also potently inhibited cell growth.

Paradoxically, in bone tissue, bazedoxifene mimics the action of estrogen, helping protect it from destruction. Because bazedoxifene has already undergone safety and efficacy studies as a treatment for osteoporosis, it may be a viable near-term option for patients with advanced breast cancer whose tumors have become resistant to other treatment options, Wardell reported. In clinical trials, the most often

reported side effect was hot flashes in the bazedoxifene treatment groups.

Provided by Duke University Medical Center